

REMARKS

I. AMENDMENTS TO THE SPECIFICATION

The specification is amended herein to capitalize the trademarks, and to introduce the generic terminology. No new matter has been added with this amendment.

II. CLAIM AMENDMENTS

Claims 1-6, 9 and 59-74 were pending in the application. Claims 1, 4, 5, 68, and 70-71 have been amended to clarify the invention. The amendments have not been made over prior art. Claims 9, 59, 62-67 and 69 have merely been amended for more descriptive claim language or for antecedent basis. No new matter has been added. Upon entry of the above-made amendments, claims 1-6, 9 and 59-71 will be pending.

Support for the claim amendments and new claims is found in the originally-filed specification, as indicated in the table below.

Claims	Examples of support in the specification
Claim 1, 4, 5, 68, 70-71	pharmacogenetically - p. 15, ll. 20 - p. 16, ll. 7; nucleic acid molecule in sample- p. 2, ll. 12-18; hybridized nucleic acid molecules that are labeled - p. 10, ll. 27- p. 11, ll. 24.
Claim 5	p. 13, ll. 16-29.

III. THE CLAIM OBJECTIONS SHOULD BE WITHDRAWN

Claims 1-6, 9, and 56-74 are objected to because claim 1 recites "one or more said particles" rather than, e.g., "said one or more particles." Applicants have amended claim 1 to recite "said one or more scattered-light detectable particles." The objection is therefore obviated and should be withdrawn.

IV. THE REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH SHOULD BE WITHDRAWN

Claims 1-6, 9, and 59-74 are rejected under 35 U.S.C. § 112, second paragraph, as indefinite over the recitation of the term "pharamcologically relevant gene." Applicants traverse the rejection because the usage of the term in the specification is consistent with the meaning of the term known in the art and one skilled in the art would understand the bounds of the claim when read in light of the specification. However, to

expedite prosecution, claims 1, 5, 68 and 70-73 have been amended to recite “pharmacogenetically relevant gene.” Support for the amendment and explanations of the terms “pharmacogenetically relevant gene” and “involved in drug metabolism” are provided in the paragraph bridging pages 15 and 16 of the specification. The amendment to the claims does not narrow the scope of the amended claim. Applicants respectfully request that the rejection of claims 1-6, 9, and 59-74 be withdrawn.

Claims 1-6, 9, and 59-74 are rejected under 35 U.S.C. § 112, second paragraph, as indefinite over the recitation of the language in step (a) of claim 1. Applicants traverse the rejection on the basis of the claims as amended. Step (a) of claim 1 has been amended to recite “wherein either said nucleic acid probe or said nucleic acid molecule is labeled with one or more scattered-light detectable particles of a size between 1 and 500 nm inclusive, thereby forming hybridized nucleic acid molecules that are labeled”. The amendment merely states explicitly the outcome of step (a) and does not narrow the scope of the amended claim. Applicants respectfully request that the rejection of claims 1-6, 9, and 59-74 be withdrawn.

Claims 1-6, 9, and 59-74 are rejected under 35 U.S.C. § 112, second paragraph, as indefinite over the recitation of the limitations “said hybridized nucleic acid molecules” and “said particle” in step (b) of claim 1. Applicants traverse the rejection on the basis of the claims as amended. Claim 1 has been amended to provide antecedent basis for the limitation “said hybridized nucleic acid molecules.” Claim 1 has also been amended to recite “one or more scattered-light detectable particles” in step (b). Applicants respectfully request that the rejection of claims 1-6, 9, and 59-74 be withdrawn.

Claims 1-6, 9, and 59-74 are rejected under 35 U.S.C. § 112, second paragraph, as indefinite over the recitation of the term “non-evanescent wave light” in claim 1. Applicants traverse the rejection because the term is well known in the art and the usage of the term in the claim is unambiguous and consistent with the art-known meaning. Briefly, evanescent wave light is generated where light traveling in one medium is totally internally reflected at an interface with a medium of a lower refractive index. Illumination by the evanescent wave light occurs in the medium of lower refractive index and only within a finite distance from the interface. The distance can be determined mathematically given the wavelength, angle of incidence and the refractive indices of the two media. Arrangements of light source and sample to achieve or to avoid evanescent light illumination are well known

to those skilled in the art. For example, United States Patent No. 5,843,651 (“the ’651 patent”, submitted as Reference AM along with the Information Disclosure Statement filed August 28, 2003), which issued on December 1, 1988, provides a detailed description of evanescent wave illumination and its application in assays (*e.g.*, the ’651 patent, Figure 1 and 3, col. 1 and 2). Thus, given the disclosure in the specification, one of skill in the art can clearly understand what is covered by the claim. The rejection is erroneous. Applicants respectfully request that the rejection of claims 1-6, 9, and 59-74 be withdrawn.

Claims 1-6, 9, and 59-74 are rejected under 35 U.S.C. § 112, second paragraph, as indefinite over the recitation of the phrase “detecting light scattered by said one or more scattered-light detectable particles under said conditions as a measure of the presence of said allele in said sample” in claim 1. Applicants traverse the rejection on the basis of the claims as amended. Claim 1 has been amended to recite “detecting light scattered by said one or more scattered-light detectable particles under said conditions which indicates the presence of said allele in said sample.” Applicants respectfully request that the rejection of claims 1-6, 9, and 59-74 be withdrawn.

Claim 2 is rejected under 35 U.S.C. § 112, second paragraph, as indefinite over the recitation of the limitation “said nucleic acid molecule in said sample.” Applicants traverse the rejection on the basis of the claims as amended. Claim 1 has been amended to provide antecedent basis for the limitation “said nucleic acid molecule in said sample” in claim 2. Applicants respectfully request that the rejection of claim 2 be withdrawn.

Claims 4 and 68-69 are rejected under 35 U.S.C. § 112, second paragraph, as indefinite over the recitation of the limitation “said nucleic acid molecule comprising said target nucleotide sequence which is not labeled with scattered-light detectable particles” in claim 4. Applicants traverse the rejection on the basis of the claims as amended. Claim 4 has been amended to recite “wherein said nucleic acid molecule is not labeled with scattered-light detectable particles.” The amendment does not narrow the scope of the amended claim. Applicants respectfully request that the rejection of claims 4 and 68-69 be withdrawn.

Claims 5 and 6 are rejected under 35 U.S.C. § 112, second paragraph, as indefinite over the recitation of the limitation “wherein said step (a) comprises contacting a plurality of different nucleic acid probes” in claim 5. Applicants traverse the rejection on the basis of the claims as amended. Claim 5 has been amended to recite “contacting the sample

with a nucleic acid probe, said method comprises contacting the sample with a plurality of different nucleic acid probes.” Applicants respectfully request that the rejection of claims 5 and 6 be withdrawn.

Claims 9 and 59-67 are rejected under 35 U.S.C. § 112, second paragraph, as indefinite over the recitation of the limitation “said nucleic acid molecules that comprise said target nucleotide sequence” in claim 9. Applicants traverse the rejection on the basis of the claims as amended. Claim 9 has been amended to recite “said nucleic acid molecule that comprise said target nucleotide sequence.” Also, claim 1 has been amended to recite “wherein said nucleic acid molecule comprises a target nucleotide sequence,” which provides antecedent basis for claim 9. The amendments do not narrow the scope of the amended claim. Applicants respectfully submit that the rejection of claims 9 and 59-67 be withdrawn.

Claims 59 and 63-67 are rejected under 35 U.S.C. § 112, second paragraph, as indefinite over the recitation of the limitation “said labeling step” in claims 59, 63-65 and 67. Applicants traverse the rejection on the basis of the claims as amended. Claims 59, 63-65 and 67 have been amended to recite “said labeling” instead of “said labeling step.” The amendment does not narrow the scope of the amended claim. Applicants respectfully submit that the rejection of claims 59 and 63-67 be withdrawn.

Claims 62 and 65 are rejected under 35 U.S.C. § 112, second paragraph, as indefinite because claims 62 and 65 allegedly do not further limit claim 61. Applicants traverse the rejection on the basis of the claims as amended. As per the Examiner’s suggestion, claim 62 has been amended to recite “wherein said incorporated moiety is a hapten-derivatized nucleotide.” Applicants respectfully submit that the rejection of claims 62 and 65 be withdrawn.

Claim 66 is rejected under 35 U.S.C. § 112, second paragraph, as indefinite over the recitation of the limitation “said target nucleotide sequence labeled with bromodeoxyuridine.” Applicants traverse the rejection on the basis of the claims as amended. Claim 66 has been amended to correct for antecedent basis and to recite “wherein said incorporated moiety is bromodeoxyuridine.” Applicants respectfully request that the rejection of claim 66 be withdrawn.

Claims 68 and 69 are rejected under 35 U.S.C. § 112, second paragraph, as indefinite over the recitation of the limitation “said step of contacting the sample with a

capture probe.” Applicants traverse the rejection on the basis of the claims as amended. Claims 68 and 69 have been amended to recite “wherein said contacting the sample.” The amendment does not narrow the scope of the amended claim. Applicants respectfully request that the rejection of claims 68 and 69 be withdrawn.

Claim 74 is canceled and thus the rejection under 35 U.S.C. § 112, second paragraph, is moot.

In view of the foregoing, Applicants respectfully request that the rejections of the claims be withdrawn. Applicants respectfully request that the amendments and remarks made herein be entered and made of record in the file history of the instant application.

Respectfully submitted,

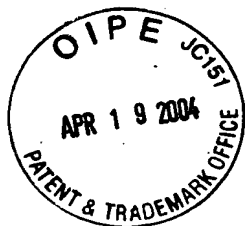
Date: April 19, 2004

Laura A. Coruzzi 30,742
Laura A. Coruzzi (Reg. No.)

By: T. Christopher Tsang 40,258
T. Christopher Tsang (Reg. No.)

JONES DAY
222 East 41st Street
New York, New York 10017-6702
(212) 790-9090

Enclosure



Annotated Sheet Showing Changes

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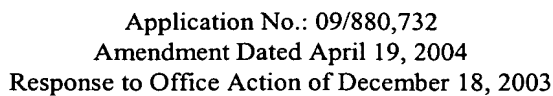
FIGURE 6A

Numbering is according to Kimura et al.

1. 'A' Allele, CYP2D6*3, A2637 deletion, Frameshift resulting in zero enzyme activity

5'-GCTAACTGAGCAGGATGACCG-3' NH2	CYPwt(+JA2624, 22mer, 54%GC, Tm=63-64C	(SEQ ID NO. 1)
5'-GCTAACTGAGCAGGATGACCG-3' NH2	CYPwt(+JA2624(A)30-3'NH2	(SEQ ID NO. 2)
5'-CTAACTGAGCAGGATGACCG-3' NH2	CYPwt(+JA2625(A)30-3'NH2	(SEQ ID NO. 3)
5'-CTAACTGAGCAGGATGACCG-3' NH2	CYPwt(+JA2625b(A)30-3'NH2	(SEQ ID NO. 4)
5'-CTAACTGAGCAGGATGACCG-3' NH2	CYPwt(+JA2625c(A)30-3'NH2	(SEQ ID NO. 5)
5'-GCTAACTGAGCAGGATGACCG-3' NH2	CYPmul(+JA2624, 21mer, 57%GC, Tm=61-63C	(SEQ ID NO. 6)
5'-GCTAACTGAGCAGGATGACCG-3' NH2	CYPmul(+JA2624(A)30-3'NH2	(SEQ ID NO. 7)
5'-CTAACTGAGCAGGATGACCG-3' NH2	CYPmul(+JA2625(A)30-3'NH2	(SEQ ID NO. 8)
5'-CTAACTGAGCAGGATGACCG-3' NH2	CYPmul(+JA2625b(A)30-3'NH2	(SEQ ID NO. 9)
5'-CTAACTGAGCAGGATGACCG-3' NH2	CYPmul(+JA2625c(A)30-3'NH2	(SEQ ID NO. 10)
5'-gctlaactgagcagcaggaatg(A)30-3' NH2	CYPwt(+JA2624b(A)30-3'NH2	(SEQ ID NO. 11)
NH23'-(A)30gactgctgctactg-5'	CYPwt(-JA2625(A)30-3'NH2	(SEQ ID NO. 12)
x= 2-Amino-dA	CYPwt(+JA2629a(A)30-3'NH2	(SEQ ID NO. 13)
x= C-5 propynyl-C	CYPwt(+JA2629b(A)30-3'NH2	(SEQ ID NO. 14)
x= C-5 propynyl-C	CYPwt(+JA2629c(A)30-3'NH2	(SEQ ID NO. 15)
5'-GCTGGATGAGCTGCTAAGCTGAGCAGGATGACCTGGGACCCAGCCCG-3'	Wild Type (+)	(SEQ ID NO. 16)
5'-GCTGGATGAGCTGCTAAGCTGAGCAGGATGACCTGGGACCCAGCCCG-3'	Mut (+)	(SEQ ID NO. 17)

deleted



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FIGURE 6D

6. 'T Allele, CYP2D6*6, T1795 deletion, Frameshift resulting in zero enzyme activity

	5'- G C T G G A G C A G T G G G T G A C -3' NH2	CYPwI(+)/J1785, 18mer, 67%GC, Tm=59-61C
	5'- G C T G G A G C A G T G G G T G A C (A)30-3' NH2	CYPwI(+)/J1785(A)30-3'NH2
	5'- C T G G A G C A G T G G G T G A C (A)30-3' NH2	CYPwI(+)/J1786(A)30-3'NH2
	5'- C T G G A G C A G - G G G T G A C -3' NH2	CYPMutl(+)/J1785, 17mer, 71%GC, Tm=58-60C
	5'- G C T G G A G C A G - G G G T G A C (A)30-3' NH2	CYPMutl(+)/J1785(A)30-3'NH2
-1773	5'- C T G G A G C A G - G G G T G A C (A)30-3' NH2	CYPMutl(+)/J1786(A)30-3'NH2
5'-GGGCAAGAAGTCGCTGGAGCAGTGGGTGACCGAGAGAGCCGCCCTGCCT-3'		Wild Type (+)
5'-GGGCAAGAAGTCGCTGGAGCAG - GGGTGACCGAGAGAGCCGCCCTGCCT-3'		Mut (+)

7. 2D6/2D7/2D8 Controls - The 2D6/7/8 probes were designed in the 1600 region of the 2D6 gene. The purpose of the designs was to find region somewhere between the PCR primers were it would be easy to discriminate between 2D6 and its two pseudogenes, 2D7 and 2D8. The purpose of the designs is to demonstrate that the PCR amplicon is from the 2D6 gene, not one of the pseudogenes.

5'-G A C C A G G G A G C - A T A G G (A)30-3' NH2	CYP2D6w(+1607)(A)30-3'NH2
5'-G A C C T T G G A G C G C A G (A)30-3' NH2	CYP2D7w(+1607)(A)30-3'NH2
5'-G A C C A G G A A A G C - A C A G G (A)30-3' NH2	CYP2D8w(+1607)(A)30-3'NH2
5'-G A C C A G G A A G C - A C A G G (A)30-3' NH2	CYP2D8w(+1607b)(A)30-3'NH2
5' G G G A C C A G G G A G C - A T A G G T T G G A G T G G G T G G T C-3' 2D6 (+)	
5' G G G A G A C C T T G T G G A G C G C A G G T T G G A G T G G G T G G T C-3' 2D7 (+)	
5' G G G A G A C C A G G A A A G C - A C A G G G T T G G A G T G G G C G G C-3' 2D8 (+)	

8. Pos/Neg Control probes. These probes were designed as true positive and negative control probes. They consist of the same semi-random sequence, with the positive control probe having a 5' Biotin.

	CYP1(+)/ran(A)25-5'Biotin, ³ NH ₂
5' Biotin-	A T C A T T C C A T C A T C C A T A T C A T C
5'-	A T C A T T C C A T C A T C C A T A T C A T C
	CYP1(+)/ran(A)25-3'NH ₂

(SEQ ID NO. 1)
(SEQ ID NO. 2)
(SEQ ID NO. 3)
(SEQ ID NO. 4)
(SEQ ID NO. 5)
(SEQ ID NO. 6)
(SEQ ID NO. 7)
(SEQ ID NO. 8)
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